

their ability to increase or decrease phosphorylation of eNOS depending on the calmodulin and calcium ion concentrations. The invention also provides a method of identifying modulators of AMPK-mediated inhibition of eNOS, comprising testing a putative modulator for its ability to decrease or increase AMPK-mediated phosphorylation of eNOS in the presence of limiting calcium ions. Preferably, specific phosphorylation of threonine 495 is assessed. The invention further provides a method of identifying modulators that either promote or inhibit phosphorylation of nNOS and nNOS μ at Ser-1417. Compounds that activate the AMP-activated protein kinase are expected to be useful in the treatment of ischemic heart disease by promoting both glucose and fatty acid metabolism, as well as by increasing NOS activity to improve nutrient and oxygen supply to the myocytes and to reduce mechanical activity. These compounds also have utility in the treatment of pulmonary hypertension and in obstructive airways disease.

At the appropriate pages, prior to the text on each page, please delete the header that reads "WO 00/28076 PCT/AU99/00968" if necessary.

In the Claims:

After entry into the U.S. national stage, and assurance of a U.S. filing date, please revise the claims from the enclosed PCT application so that the rewritten claims read as follows:

5. (Amended) A method according to Claim 1, in which one or more of the following activities is additionally assessed:

- (a) Effect on smooth muscle contraction;
- (b) Effect on inotropic activity of the heart;
- (b) Effect on chronotropic activity of the heart; or